FIGURE 1

In Vitro Deposition Pattern of Aerosolized BDP Dispersions

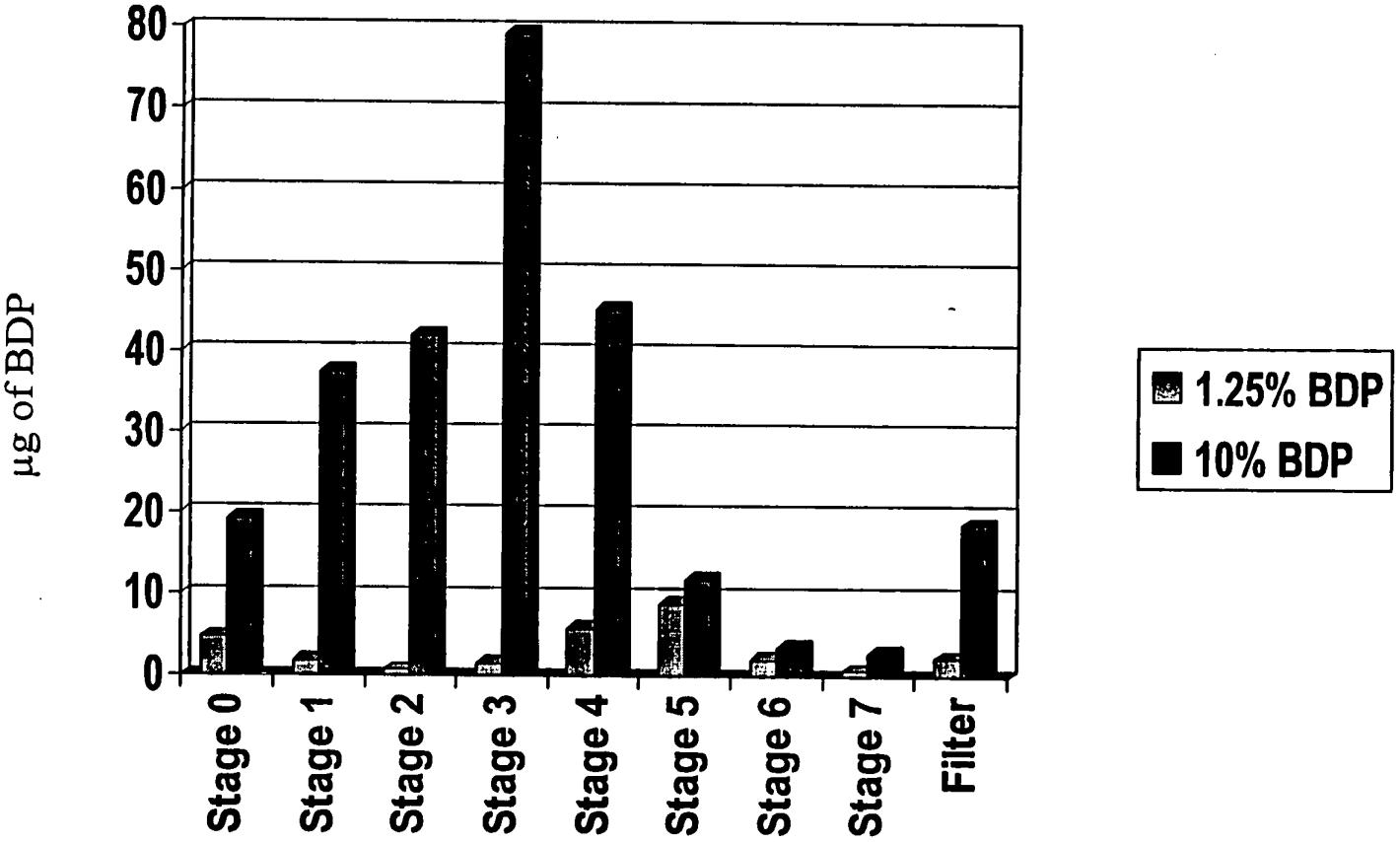


FIGURE 2

In Vitro Deposition Pattern of Nanoparticulate BDP Suspensions

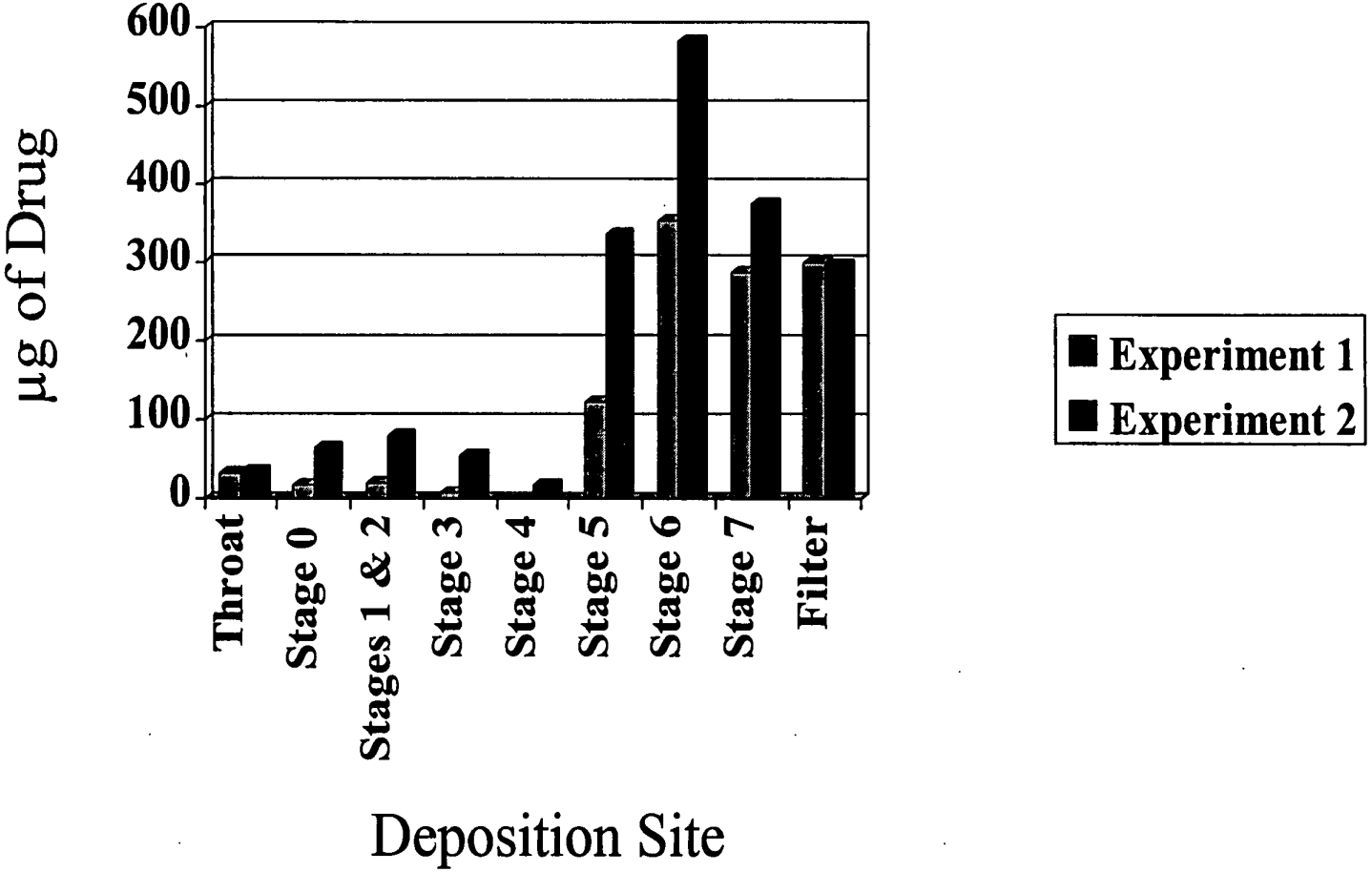
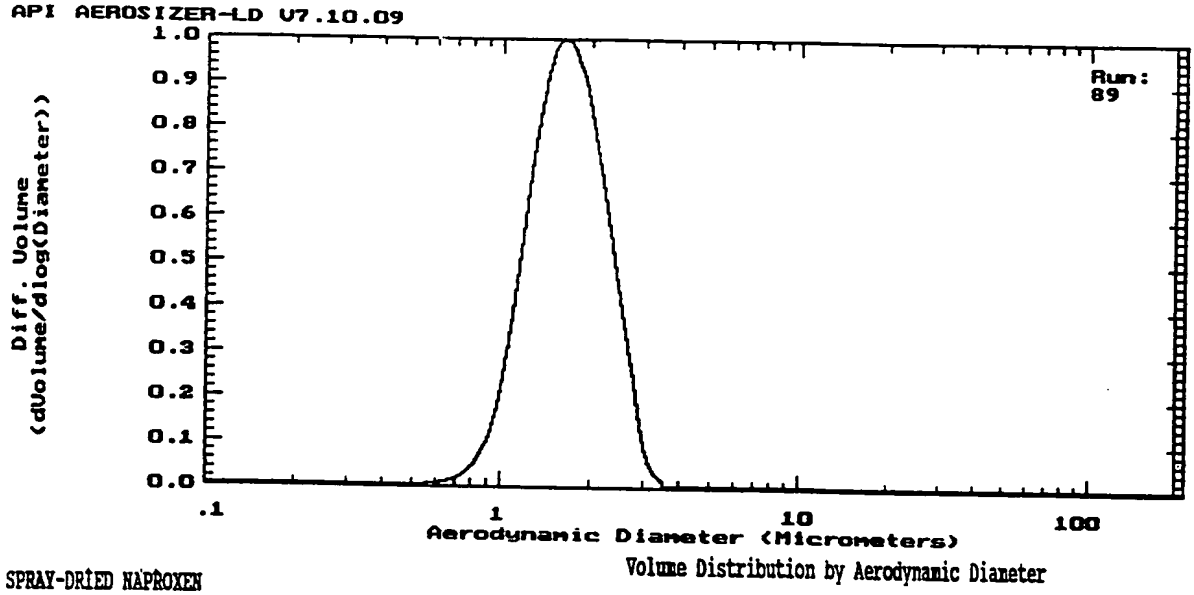


FIGURE 3



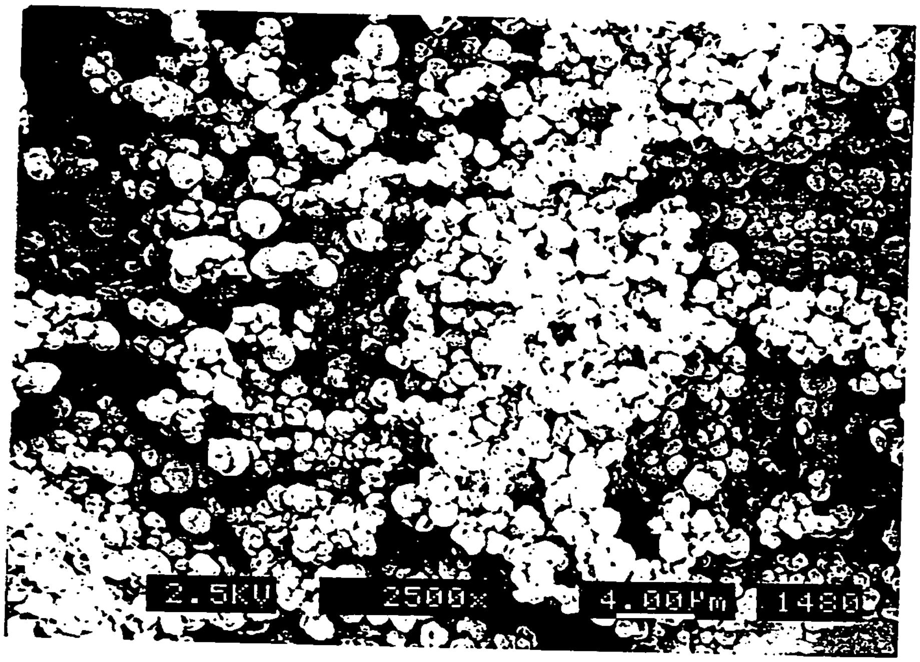
SPRAY-DRIED NAPROXEN

Volume Distribution by Aerodynamic Diameter

STATISTICS			PARAMETERS		%UNDER	SIZE	%UNDER	SIZE
Mean Size	: 1.671		Material	: SDI-naproxen	10%	1.157	90%	2.432
Standard Deviation	: 1.334		Density	: 1.26	50%	1.675		
D(4,3)	: 1.740		Run Length (sec)	: 123.9				
D(3,2)	: 1.602		PMT Voltage	: 1100.0				
Mode (Log Scale)	: 1.65		Sum of channels	: 46211				
Specific Surface Area	: 2.97	sq meter/g	Lower Size Limit	: 0.10				
			Upper Size Limit	: 200.00				
			Nozzle Type	: 700um				
			Baseline Offset	: 0.10				
			Noise Filter	: 6.00				
			Regularization	: Low				

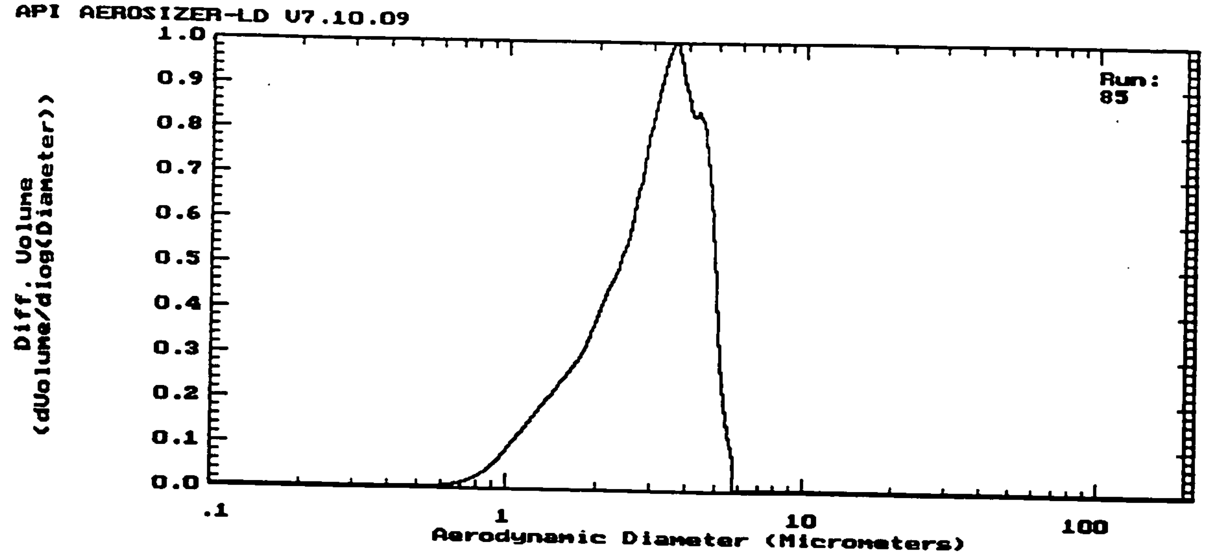
UPPER SIZE	% IN	LOWER SIZE	% UNDER	UPPER SIZE	% IN	LOWER SIZE	% UNDER	UPPER SIZE	% IN	LOWER SIZE	% UNDER	UPPER SIZE	% IN	LOWER SIZE	% UNDER
				100	0.0000	86.0	100.00	10.0	0.0000	8.60	100.00	1.00	2.4683	0.86	1.2857
				86.0	0.0000	74.0	100.00	8.60	0.0000	7.40	100.00	0.86	0.8394	0.74	0.4463
				74.0	0.0000	63.0	100.00	7.40	0.0000	6.30	100.00	0.74	0.3050	0.63	0.1413
				63.0	0.0000	54.0	100.00	6.30	0.0000	5.40	100.00	0.63	0.1042	0.54	0.0371
				54.0	0.0000	46.0	100.00	5.40	0.0000	4.60	100.00	0.54	0.0333	0.46	0.0038
				46.0	0.0000	40.0	100.00	4.60	0.0000	4.00	100.00	0.46	0.0036	0.40	0.0003
				40.0	0.0000	34.0	100.00	4.00	0.1153	3.40	99.885	0.40	0.0003	0.34	0.0000
				34.0	0.0000	29.0	100.00	3.40	1.7044	2.90	98.180	0.34	0.0000	0.29	0.0000
				29.0	0.0000	25.0	100.00	2.90	6.4095	2.50	91.771	0.29	0.0000	0.25	0.0000
				25.0	0.0000	22.0	100.00	2.50	9.8151	2.20	81.956	0.25	0.0000	0.22	0.0000
				22.0	0.0000	18.0	100.00	2.20	22.597	1.80	59.359	0.22	0.0000	0.18	0.0000
180	0.0000	160	100.00	18.0	0.0000	16.0	100.00	1.80	15.436	1.60	43.923	0.18	0.0000	0.16	0.0000
160	0.0000	140	100.00	16.0	0.0000	14.0	100.00	1.60	16.757	1.40	27.166	0.16	0.0000	0.14	0.0000
140	0.0000	120	100.00	14.0	0.0000	12.0	100.00	1.40	14.681	1.20	12.484	0.14	0.0000	0.12	0.0000
120	0.0000	100	100.00	12.0	0.0000	10.0	100.00	1.20	8.7303	1.00	3.7540	0.12	0.0000	0.10	0.0000

FIGURE 4



Spray Dried Nanoparticulate Naproxen

FIGURE 5



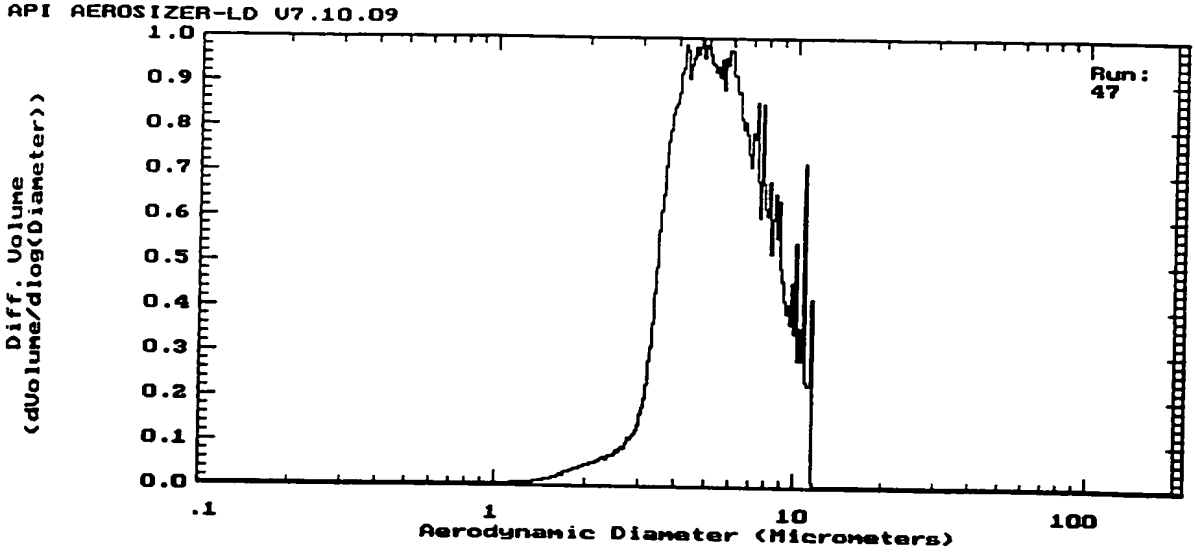
SPRAY-DRIED NAPROXEN

Volume Distribution by Aerodynamic Diameter

STATISTICS		PARAMETERS		%UNDER	SIZE	%UNDER	SIZE
Mean Size	: 2.906	Material	: SDI-naproxen	10%	1.554	90%	4.651
Standard Deviation	: 1.524	Density	: 1.26	50%	3.183		
D(4,3)	: 3.142	Run Length (sec)	: 108.9				
D(3,2)	: 2.632	PMT Voltage	: 1100.0				
Mode (Log Scale)	: 3.66	Sum of channels	: 13520				
Specific Surface Area	: 1.81 sq meter/g	Lower Size Limit	: 0.10				
		Upper Size Limit	: 200.00				
		Nozzle Type	: 700um				
		Baseline Offset	: 0.10				
		Noise Filter	: 6.00				
		Regularization	: Low				

UPPER SIZE	% IN	LOWER SIZE	% UNDER	UPPER SIZE	% IN	LOWER SIZE	% UNDER	UPPER SIZE	% IN	LOWER SIZE	% UNDER	UPPER SIZE	% IN	LOWER SIZE	% UNDER
				100	0.0000	86.0	100.00	10.0	0.0000	8.60	100.00	1.00	1.0101	0.86	0.6844
				86.0	0.0000	74.0	100.00	8.60	0.0000	7.40	100.00	0.86	0.4335	0.74	0.2509
				74.0	0.0000	63.0	100.00	7.40	0.0000	6.30	100.00	0.74	0.1785	0.63	0.0723
				63.0	0.0000	54.0	100.00	6.30	1.1614	5.40	98.839	0.63	0.0548	0.54	0.0175
				54.0	0.0000	46.0	100.00	5.40	9.8645	4.60	88.974	0.54	0.0153	0.46	0.0021
				46.0	0.0000	40.0	100.00	4.60	13.706	4.00	75.268	0.46	0.0020	0.40	0.0001
				40.0	0.0000	34.0	100.00	4.00	18.274	3.40	56.994	0.40	0.0001	0.34	0.0000
				34.0	0.0000	29.0	100.00	3.40	15.715	2.90	41.278	0.34	0.0000	0.29	0.0000
				29.0	0.0000	25.0	100.00	2.90	10.821	2.50	30.457	0.29	0.0000	0.25	0.0000
				25.0	0.0000	22.0	100.00	2.50	7.2247	2.20	23.232	0.25	0.0000	0.22	0.0000
				22.0	0.0000	18.0	100.00	2.20	8.6259	1.80	14.606	0.22	0.0000	0.18	0.0000
180	0.0000	160	100.00	18.0	0.0000	16.0	100.00	1.80	3.7744	1.60	10.832	0.18	0.0000	0.16	0.0000
160	0.0000	140	100.00	16.0	0.0000	14.0	100.00	1.60	3.5448	1.40	7.2871	0.16	0.0000	0.14	0.0000
140	0.0000	120	100.00	14.0	0.0000	12.0	100.00	1.40	3.1759	1.20	4.1112	0.14	0.0000	0.12	0.0000
120	0.0000	100	100.00	12.0	0.0000	10.0	100.00	1.20	2.4167	1.00	1.6945	0.12	0.0000	0.10	0.0000

FIGURE 6



Volume Distribution by Aerodynamic Diameter

spray dried ta

STATISTICS		PARAMETERS		%UNDER	SIZE	%UNDER	SIZE
Mean Size	: 5.540	Material	: SDI-naproxen	10%	3.600	90%	9.082
Standard Deviation	: 1.455	Density	: 1.26	50%	5.516		
D(4,3)	: 5.924	Run Length (sec)	: 189.6				
D(3,2)	: 5.146	PMT Voltage	: 1100.0				
Mode (Log Scale)	: 4.82	Sum of channels	: 100494				
Specific Surface Area	: 0.93 sq meter/g	Lower Size Limit	: 0.10				
		Upper Size Limit	: 200.00				
		Nozzle Type	: 700um				
		Baseline Offset	: 0.10				
		Noise Filter	: 6.00				
		Regularization	: Off				

UPPER SIZE	% IN	LOWER SIZE	% UNDER	UPPER SIZE	% IN	LOWER SIZE	% UNDER	UPPER SIZE	% IN	LOWER SIZE	% UNDER	UPPER SIZE	% IN	LOWER SIZE	% UNDER
				100	0.0000	86.0	100.00	10.0	7.5026	8.60	86.677	1.00	0.0237	0.86	0.0213
				86.0	0.0000	74.0	100.00	8.60	10.326	7.40	76.352	0.86	0.0121	0.74	0.0092
				74.0	0.0000	63.0	100.00	7.40	13.417	6.30	62.935	0.74	0.0064	0.63	0.0028
				63.0	0.0000	54.0	100.00	6.30	14.999	5.40	47.935	0.63	0.0021	0.54	0.0006
				54.0	0.0000	46.0	100.00	5.40	16.094	4.60	31.841	0.54	0.0006	0.46	0.0001
				46.0	0.0000	40.0	100.00	4.60	13.547	4.00	18.295	0.46	0.0001	0.40	0.0000
				40.0	0.0000	34.0	100.00	4.00	11.255	3.40	7.0394	0.40	0.0000	0.34	0.0000
				34.0	0.0000	29.0	100.00	3.40	3.2799	2.90	3.7595	0.34	0.0000	0.29	0.0000
				29.0	0.0000	25.0	100.00	2.90	1.3355	2.50	2.4240	0.29	0.0000	0.25	0.0000
				25.0	0.0000	22.0	100.00	2.50	0.8131	2.20	1.6109	0.25	0.0000	0.22	0.0000
				22.0	0.0000	18.0	100.00	2.20	0.8995	1.80	0.7114	0.22	0.0000	0.18	0.0000
180	0.0000	160	100.00	18.0	0.0000	16.0	100.00	1.80	0.3128	1.60	0.3985	0.18	0.0000	0.16	0.0000
160	0.0000	140	100.00	16.0	0.0000	14.0	100.00	1.60	0.1861	1.40	0.2125	0.16	0.0000	0.14	0.0000
140	0.0000	120	100.00	14.0	0.0000	12.0	100.00	1.40	0.1061	1.20	0.1063	0.14	0.0000	0.12	0.0000
120	0.0000	100	100.00	12.0	5.8201	10.0	94.180	1.20	0.0613	1.00	0.0450	0.12	0.0000	0.10	0.0000

FIGURE 7(A)

Spray-dried nanoparticulate budesonide

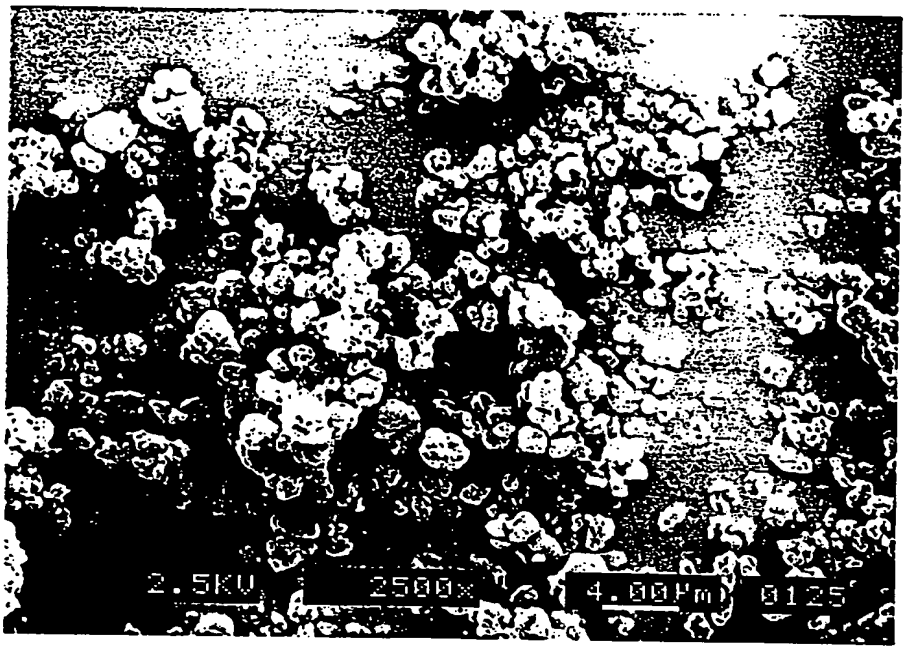


FIGURE 7(B)

Micronized budesonide

FIGURE 8

HORIBA LA-910

Laser scattering particle size distribution analyzer

PARTICLE SIZE MEASUREMENT DATA

Freeze-dried

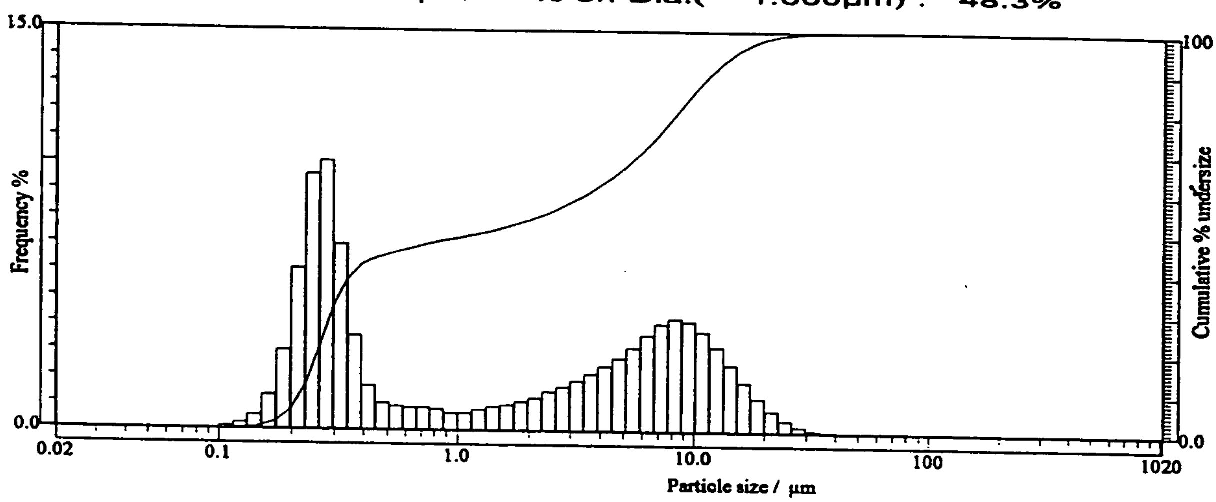
Material : 5%Dextrose 4-3-98
Source : Reconst. water/3g fill
Lot Numbe : in water/1 min. sonication

Data

Median : 1.355μm SP.Area: 114884cm²/cm³ S.D. : 5.324μm
Mode : 0.272μm Mean : 4.225μm
C.V. : 126.02%

Span : (D 10.0-D 90.0) / D50 = 8.564

Dia. on %(90.0%) :	11.822μm	% on Dia.(0.400μm) :	41.9%
Dia. on %(50.0%) :	1.355μm	% on Dia.(0.300μm) :	31.7%
Dia. on %(95.0%) :	14.996μm	% on Dia.(0.100μm) :	0.0%
Dia. on %(80.0%) :	8.384μm	% on Dia.(0.200μm) :	5.9%
Dia. on %(70.0%) :	5.949μm	% on Dia.(1.000μm) :	48.3%



Size(μm)	Freq(%)	Und(%)
1019.5	0.00	100.00
890.1	0.00	100.00
777.1	0.00	100.00
678.5	0.00	100.00
592.4	0.00	100.00
517.2	0.00	100.00
451.6	0.00	100.00
394.2	0.00	100.00
344.2	0.00	100.00
300.5	0.00	100.00
262.4	0.00	100.00
229.1	0.00	100.00
200.0	0.00	100.00
174.6	0.00	100.00
152.5	0.00	100.00
133.1	0.00	100.00
116.2	0.00	100.00
101.5	0.00	100.00
88.58	0.00	100.00
77.34	0.00	100.00
67.52	0.00	100.00
58.95	0.00	100.00
51.47	0.00	100.00
44.94	0.00	100.00
39.23	0.00	100.00
34.25	0.11	100.00
29.91	0.24	99.89

Size(μm)	Freq(%)	Und(%)
26.11	0.46	99.66
22.80	0.81	99.20
19.90	1.29	98.39
17.38	1.88	97.10
15.17	2.54	95.22
13.25	3.20	92.68
11.56	3.76	89.48
10.10	4.15	85.72
8.816	4.26	81.57
7.697	4.06	77.32
6.720	3.63	73.26
5.867	3.16	69.63
5.122	2.76	66.47
4.472	2.46	63.71
3.905	2.16	61.25
3.409	1.89	59.10
2.976	1.68	57.21
2.599	1.49	55.52
2.269	1.24	54.03
1.981	1.10	52.79
1.729	0.97	51.69
1.510	0.90	50.72
1.318	0.80	49.82
1.151	0.67	49.02
1.005	0.66	48.35
0.877	0.81	47.69
0.766	0.86	46.88

Size(μm)	Freq(%)	Und(%)
0.669	0.86	46.02
0.584	0.90	45.16
0.510	1.03	44.26
0.445	1.68	43.23
0.389	3.56	41.54
0.339	6.97	37.98
0.296	10.10	31.01
0.259	9.61	20.91
0.226	6.06	11.30
0.197	2.99	5.23
0.172	1.31	2.24
0.150	0.56	0.93
0.131	0.26	0.37
0.115	0.11	0.11
0.100	0.00	0.00
0.087	0.00	0.00
0.076	0.00	0.00
0.067	0.00	0.00
0.058	0.00	0.00
0.051	0.00	0.00
0.044	0.00	0.00
0.039	0.00	0.00
0.034	0.00	0.00
0.029	0.00	0.00
0.026	0.00	0.00
0.022	0.00	0.00

FIGURE 9

HORIBA LA-910

Laser scattering particle size distribution analyzer

PARTICLE SIZE MEASUREMENT DATA

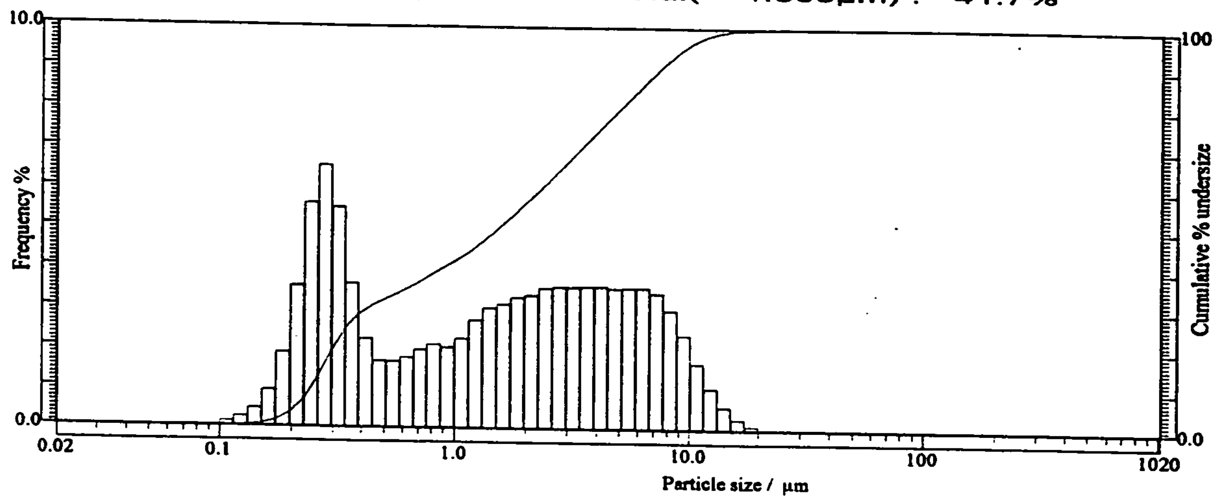
Material : reconst. 1%N9585. 5%Man
Source : in water
Lot Numbe : 1min sonication

Data

Median : 1.533µm SP.Area: 93485cm²/cm³ S.D. : 3.123µm
Mode : 0.276µm Mean : 2.767µm
C.V. : 112.86%

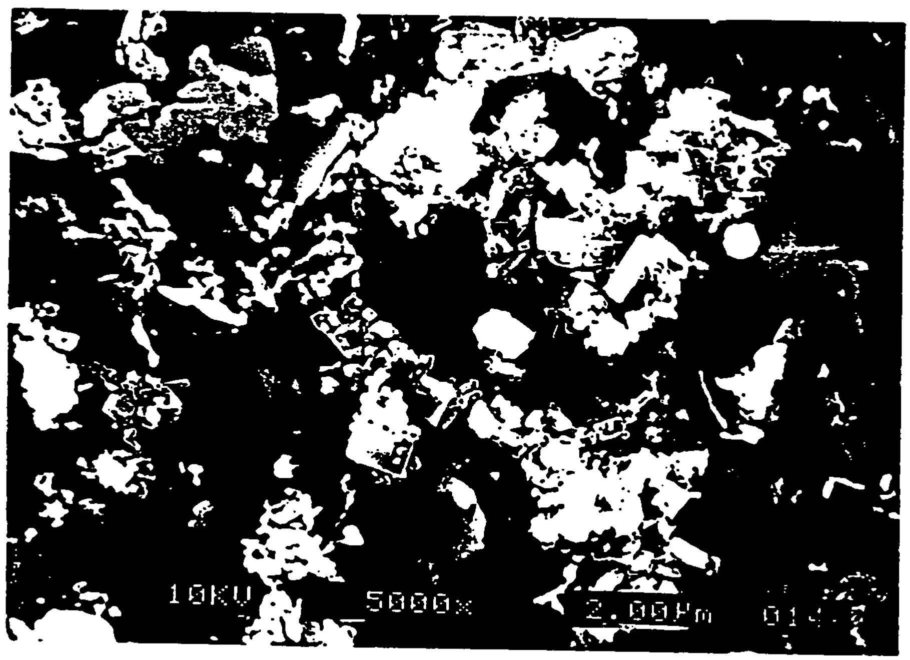
Span : (D 10.0-D 90.0) / D50 = 4.665

Dia. on %(90.0%) :	7.392µm	% on Dia.(0.400µm) :	28.8%
Dia. on %(50.0%) :	1.533µm	% on Dia.(0.300µm) :	19.8%
Dia. on %(95.0%) :	9.346µm	% on Dia.(0.100µm) :	0.0%
Dia. on %(80.0%) :	5.011µm	% on Dia.(0.200µm) :	4.0%
Dia. on %(70.0%) :	3.416µm	% on Dia.(1.000µm) :	41.7%



Size(µm)	Freq(%)	Und(%)	Size(µm)	Freq(%)	Und(%)	Size(µm)	Freq(%)	Und(%)
1019.5	0.00	100.00	26.11	0.00	100.00	0.669	1.75	35.66
890.1	0.00	100.00	22.80	0.00	100.00	0.584	1.65	33.91
777.1	0.00	100.00	19.90	0.11	100.00	0.510	1.67	32.26
678.5	0.00	100.00	17.38	0.27	99.89	0.445	2.22	30.59
592.4	0.00	100.00	15.17	0.57	99.61	0.389	3.60	28.36
517.2	0.00	100.00	13.25	1.04	99.04	0.339	5.49	24.76
451.6	0.00	100.00	11.56	1.66	98.00	0.296	6.54	19.28
394.2	0.00	100.00	10.10	2.35	96.34	0.259	5.59	12.74
344.2	0.00	100.00	8.816	2.98	93.99	0.226	3.52	7.15
300.5	0.00	100.00	7.697	3.38	91.01	0.197	1.87	3.63
262.4	0.00	100.00	6.720	3.53	87.62	0.172	0.93	1.76
229.1	0.00	100.00	5.867	3.52	84.09	0.150	0.46	0.84
200.0	0.00	100.00	5.122	3.51	80.57	0.131	0.25	0.38
174.6	0.00	100.00	4.472	3.55	77.06	0.115	0.13	0.13
152.5	0.00	100.00	3.905	3.56	73.50	0.100	0.00	0.00
133.1	0.00	100.00	3.409	3.53	69.94	0.087	0.00	0.00
116.2	0.00	100.00	2.976	3.54	66.41	0.076	0.00	0.00
101.5	0.00	100.00	2.599	3.51	62.87	0.067	0.00	0.00
88.58	0.00	100.00	2.269	3.33	59.36	0.058	0.00	0.00
77.34	0.00	100.00	1.981	3.27	56.03	0.051	0.00	0.00
67.52	0.00	100.00	1.729	3.10	52.76	0.044	0.00	0.00
58.95	0.00	100.00	1.510	3.00	49.66	0.039	0.00	0.00
51.47	0.00	100.00	1.318	2.70	46.66	0.034	0.00	0.00
44.94	0.00	100.00	1.151	2.24	43.96	0.029	0.00	0.00
39.23	0.00	100.00	1.005	2.02	41.73	0.026	0.00	0.00
34.25	0.00	100.00	0.877	2.09	39.71	0.022	0.00	0.00
29.91	0.00	100.00	0.766	1.95	37.62			

FIGURE 10



**Micrograph of
Milled TA (3.6%) with Span 85 (0.5%)**